

Amendments to the Claims:

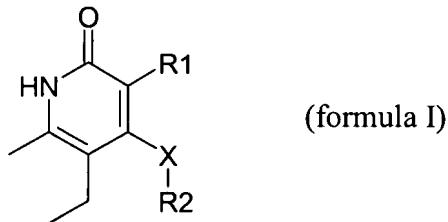
This listing of claims will replace all prior versions and listings of claims in the application.

Claims 2-8, 12-14, 16 and 17 are amended.

Claim 18 is new

Listing of Claims:

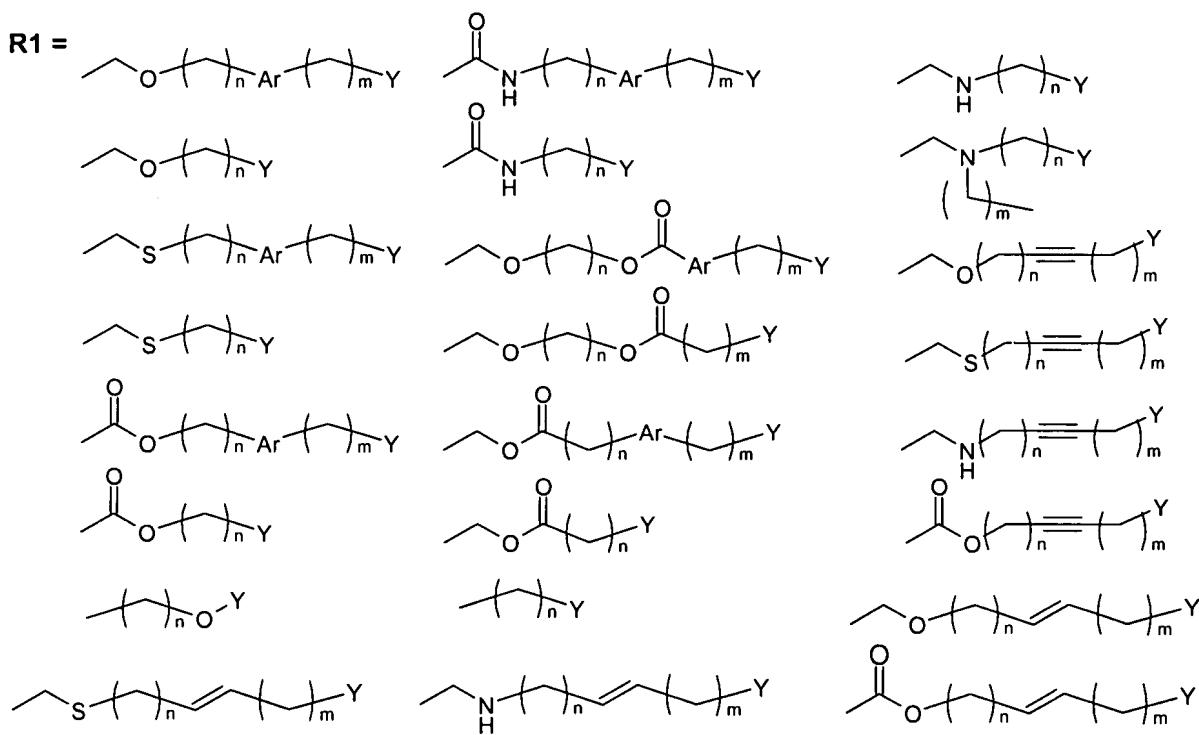
1. (Original) A 5-ethyl-6-methyl-2-pyridinone derivative compound according to general formula I,



wherein

X = O, S, NH, C=O, (C_nH_{2n}), (C_nH_{2n})O, O(C_nH_{2n}), (C_nH_{2n})S, S(C_nH_{2n}) with n = 1-4

R1 =

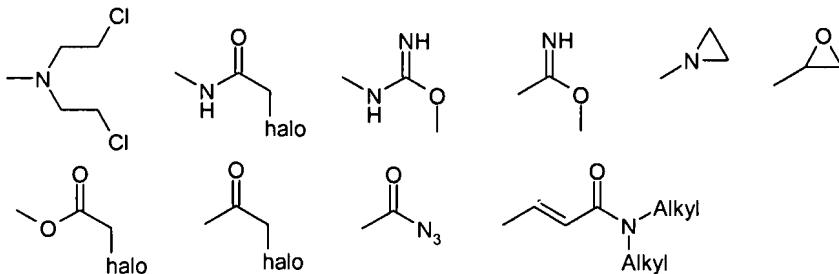


with n, m = 0 - 8

Ar = Aromatic ring selected from : phenyl, pyridyl, thiazolyl, furanyl, thiophenyl, benzofuranyl, benzothiophenyl, benzothiazolyl, imidazolyl, indolyl, each optionally substituted with up to 4 substituants selected from : halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ hydroxyalkyl, C₁₋₄ alkylamino, amino, C₁₋₄ aminoalkyl, C₁₋₄ alkylcarbonyl, C₁₋₄ dialkylamino, azido

Y = alkyl, amino, nitro or

Y = H, halo, alkylamino, dialkylamino, nitrile, hydroxy, C₁₋₆alkyloxycarbonyl, C₁₋₆alkylcarbonyloxy, C₅₋₇ cycloalkyl optionally substituted with up to 4 substituants selected from :
halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ hydroxyalkyl, C₁₋₄ alkylamino, amino, C₁₋₄ aminoalkyl, C₁₋₄ alkylcarbonyl, C₁₋₄ dialkylamino, azido, nitrile;
or Y can be :



R2 = C₇₋₉ cycloalkyl;

C₅₋₈ cycloalkyl substituted with up to 4 substituants;

C₅₋₈cycloalkenyl optionally substituted with up to 4 substituants;

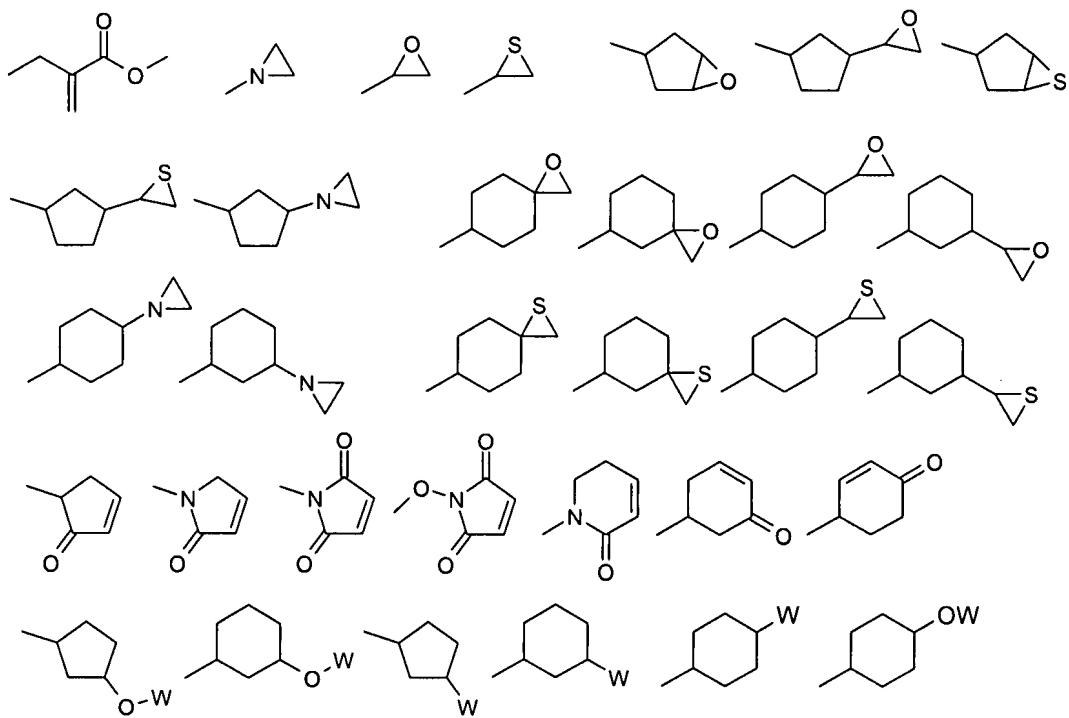
C₅₋₈aliphatic heterocycle optionally substituted with up to 4 substituants;

C₆₋₉bridged cycloalkyl optionally substituted with up to 4 substituants;

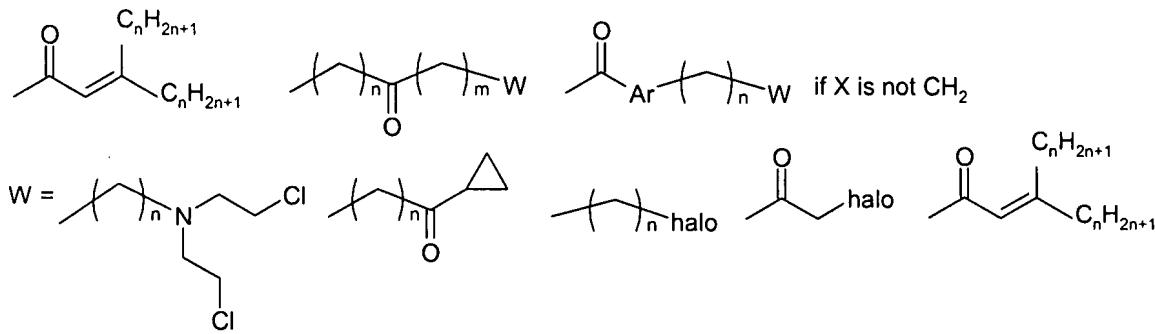
C₆₋₉bridged cycloalkenyl optionally substituted with up to 4 substituants;

substituants selected from :

halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ hydroxyalkyl, C₁₋₄ alkylamino, amino, C₁₋₄ aminoalkyl, C₁₋₄ alkylcarbonyl, C₁₋₄ dialkylamino, azido, CN;



Or R2 can be :



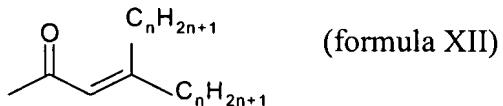
$n, m = 0 - 8$

2. (Currently Amended) The compound according to claim 1 ~~further characterized in that it has~~ which comprises a substituted cycloalkyl group as R2 in position 4 of the pyridinone ring.

3. (Currently Amended) The compound according to claim 2 ~~further characterized in that said~~ wherein the substituted cycloalkyl group is a 3,5-dimethylcyclohexyl moiety.

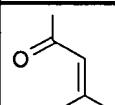
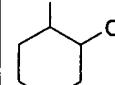
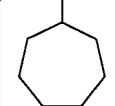
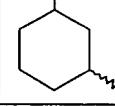
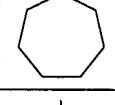
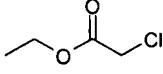
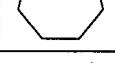
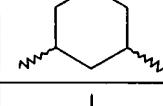
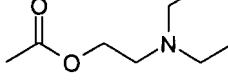
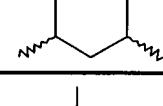
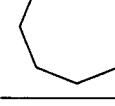
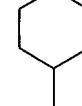
4. (Currently Amended) The compound according to claim 1 ~~further characterized in that it has~~ which comprises a C7-9 cycloalkyl group as R2 in position 4 of the pyridinone ring.

5. (Currently Amended) The compound according to claim 1 ~~further characterized in that wherein R2 accords to~~ has the formula XII

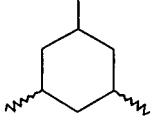


with n=0 – 8, ~~preferably n=0, 1, 2, 3 or 4, more preferably n=0, 1, or 2 and most preferably n=1.~~

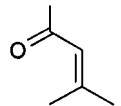
6. (Currently Amended) The compound according to claim 1 which is selected from the group[[s]] consisting of **M18**, **Z12**, **Z25**, **Z30**, **Z32**, **Z33**, **Z37**, **Z37inv**, **Z53**, **Z54**, **Z55**, **Z57**, **Z45inv**, **Z91inv**, **Z96inv**, **Z114**, **Z121**, **Z122**, **Z150**, **Z153**, **Z154** and **Z167**, wherein X, R1 and R2 are as indicated below:

Nº	X	R1	R2
M18	O	CO ₂ Et	
Z12	O	CO ₂ Et	
Z25	O	CO ₂ Et	
Z30	O	CO ₂ Et	
Z32	O	CH ₂ OH	
Z33	O		
Z37	O	CO ₂ Et	
Z53	O		
Z54	O	CO ₂ Et	
Z55	O	CO ₂ Et	

Z57		CO ₂ Et	
Z45inv	O	CH ₂ OH	
Z91inv	O	NO ₂	
Z96inv	O	NH ₂	
Z114	O	CH ₂ SCOMe	
Z121	O	CH ₂ S(CH ₂) ₂ OH	
Z122	O	CH ₂ S(CH ₂) ₂ OCOCH ₂ Cl	
Z150	O	NMe ₂	
Z153	O	CH ₂ N ₃	
Z154	O	Me	

Z167	O	Et	
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7. (Currently Amended) A compound (M18) according to claim 1,



with X = O, R1 = CO₂Et and R2 = .

8. (Currently Amended) A pharmaceutical composition comprising at least one the compound[[s]] according to any of claims the claim 1 to 7 and an acceptable carrier and/or diluent.

9. (Original) The composition according to claim 8 further comprising another anti-viral agent.

10. (Currently Amended) The composition according to claim 9, characterized in that wherein the said anti-viral agent is Nevirapine.

11. (Currently Amended) Use of the compound or the composition according to any of the preceding claims 1 to 10 for the preparation of a medicament in the treatment and/or the prevention of HIV-1 infections. A method for the treatment and/or the prevention of HIV-1 infections in a mammal, which comprises the step of administrating the compound of claim 1 or the composition of claim 8 to the mammal.

12. (Currently Amended) The use-method according to the claim 11 for the preparation of a medicament for the treatment and/or prevention of HIV-1 infections by a strain resistant to at least one anti-viral agent.

13. (Currently Amended) The use-method of claim 12 wherein said anti-viral agent is Nevirapine.

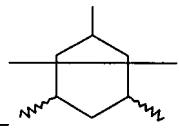
14. (Currently Amended) A method for obtaining an irreversible anti-HIV-1 compound, which ~~method~~ comprises the steps of:

- selecting an anti-HIV-1 compound, ~~preferably a NNRTI~~, that interacts with a binding site of an HIV-1 enzyme,
- introducing a chemical modification in the structure of ~~said~~ the anti-HIV-1 compound that allows the formation of at least one covalent bond between the compound and an amino acid of said HIV-1 enzyme.

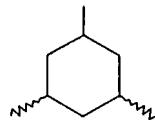
15. (Original) The method of claim 14, wherein the HIV I binding site is the allosteric site of HIV I reverse transcriptase.

16. (Currently Amended) ~~An irreversible NNRTI obtainable by said method~~ The method of claim 14 wherein the anti-HIV-1 compound is an NNRTI.

17. (Currently Amended) ~~The irreversible NNRTI according to claim 17 which is a compound (Z122) according to formula I with X = O, R1 =~~

~~CH₂S(CH₂)₂OCOCH₂Cl and R2 =~~  An irreversible NNRTI obtainable by the method of claim 16.

18. (New) The irreversible NNRTI according to claim 17 which is a compound (Z122) according to formula I with X = O, R1 = CH₂S(CH₂)₂OCOCH₂Cl and R2 =



Abstract

The present invention relates to 2-Pyridinone derivatives, more specifically 5-ethyl-6-methyl-2-pyridinone derivatives, according to general formula I that inhibit human immunodeficiency virus type 1 (HIV-1) replication and are therefore of interest in the treatment of Acquired Immune Deficiency Syndrome (AIDS). The present invention further relates to the synthesis of said compounds and their use, with or without other pharmaceutical agents, in the treatment of AIDS and viral infections by HIV-1.